Licensure of a High-Dose Inactivated Influenza Vaccine for Persons Aged ≥65 Years (Fluzone High-Dose) and Guidance for Use --- United States, 2010

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Persons aged ≥65 years are at greater risk for hospitalization and death from seasonal influenza compared with other age groups (*1,2*), and they respond to vaccination with lower antibody titers to influenza hemagglutinin (an established correlate of protection against influenza) compared with younger adults (*3*). On December 23, 2009, the Food and Drug Administration (FDA) licensed an injectable inactivated trivalent influenza vaccine (Fluzone High-Dose, Sanofi-Pasteur) that contains an increased amount of influenza virus hemagglutinin antigen compared with other inactivated influenza vaccines such as Fluzone. Fluzone High-Dose is licensed as a single dose for use among persons aged ≥65 years and will be available beginning with the 2010--11 influenza season. The Advisory Committee on Immunization Practices (ACIP) reviewed data from prelicensure clinical trials on the safety and immunogenicity of Fluzone High-Dose and expressed no preference for the new vaccine over other inactivated trivalent influenza vaccines (*4*). This report summarizes the FDA-approved indications for Fluzone High-Dose and provides guidance from ACIP for its use.

Standard dose inactivated trivalent influenza vaccines contain a total of 45 μg (15 μg of each of the three recommended strains) of influenza virus hemagglutinin antigen per 0.5mL dose (*5*). In contrast, Fluzone High-Dose is formulated to contain a total of 180 μg (60 μg of each strain) of influenza virus hemagglutinin antigen in each 0.5mL dose. Like other inactivated influenza vaccines, Fluzone High-Dose is administered as an intramuscular injection (*6*). Fluzone High-Dose is available as a single-dose prefilled syringe formulation and is distinguished from Fluzone by a gray syringe plunger rod. As with other 2010--11 influenza vaccines, Fluzone High-Dose will contain antigens of the three recommended virus strains: A/California/7/2009 (H1N1)-like, A/Perth/16/2009 (H3N2)-like, and B/Brisbane/60/2008-like (*7*).

Immunogenicity data from three studies among persons aged ≥65 years indicated that, compared with standard dose Fluzone, preparations of Fluzone High-Dose elicited significantly higher hemagglutination inhibition (HI) titers against all three influenza virus strains that were included in seasonal influenza vaccines recommended during the study period (*8--10*). In one study, prespecified criteria for superiority, defined as when the lower 95% confidence limit of 1) a ratio of geometric mean HI titers is >1.5 for at least two strains and 2) the difference in fourfold rise of HI titers is >10% for at least two strains, were demonstrated for persons aged ≥65 years who received Fluzone High-Dose compared with Fluzone for influenza A(H1N1) and influenza A(H3N2) antigens. Prespecified criteria for noninferiority to Fluzone were demonstrated for the influenza B antigen (*6,9*). Whether the higher postvaccination immune responses observed among Fluzone High-Dose vaccine recipients will result in greater protection against influenza illness is unknown.

Solicited injection site reactions and systemic adverse events were more frequent after vaccination with Fluzone High-Dose compared with standard Fluzone, but typically were mild and transient (*8--10*). In the largest study, 915 (36%) of 2,572 persons who received Fluzone High-Dose, compared with 306 (24%) of 1,275 persons who received Fluzone, reported injection site pain ≤7 days after vaccine administration. In the same study, significantly more Fluzone High-Dose recipients (1.1%) reported moderate (>100.4°F--≤102.2°F [>38°C--≤39°C]) to severe (>102.2°F [>39°C]) fever, compared with Fluzone recipients (0.3%)(*9*).

ACIP Guidance for Use of Fluzone High-Dose

Fluzone High-Dose may be used for persons aged ≥65 years. All persons aged ≥6 months are recommended for annual influenza vaccination beginning with the 2010--11 influenza season. ACIP has not expressed a preference for any specific licensed inactivated trivalent influenza vaccine, including Fluzone High-Dose, for use in persons aged ≥65 years (*4*). Data demonstrating greater protection against influenza illness after vaccination with Fluzone High-Dose are needed to evaluate whether Fluzone High-Dose is a more effective vaccine for persons aged ≥65 years. A 3-year postlicensure study of the vaccine effectiveness of Fluzone High-Dose compared with standard dose inactivated influenza vaccine (Fluzone) was begun in 2009 and should be completed in 2012. As with other inactivated influenza vaccines, Fluzone High-Dose should not be administered to anyone with a known hypersensitivity to egg proteins or influenza vaccine. Adverse events after receipt of any vaccine should be reported to the Vaccine Adverse Event Reporting System at http://vaers.hhs.gov.

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